

Dietmar Spengler and Laurent Journot
U.S. Serial No.: 09/254,870
Filed: August 16, 1999
Page 2

Please amend the subject application as follows:

In the Specification

Please amend the specification by deleting the paragraph on page 1, lines 1-4, and inserting the following paragraph:

D₁
~~(Now)~~ This application is a national stage application filed under 35 U.S.C. §371 of PCT International Application No. PCT/EP97/05198, filed September 22, 1997, which designated the United States of America as a continuation-in-part of U.S. Serial No. 08/718,661, filed September 23, 1996, now U.S. Patent No. 5,876,972, issued March 2, 1999. The contents of these applications are incorporated herein by reference.

In the Claims

Please cancel claims 1-16 and 41 without prejudice or disclaimer to applicants' right to pursue the subject matter of these claims in a future continuation or divisional application.

Please amend claims 17-20, 36 and 39 as follows:

D₂
17. (Amended) A nucleic acid molecule encoding a protein having the biological activity of a tumor suppressor, wherein the nucleic acid molecule comprises (a) a nucleotide sequence encoding the amino acid sequence given in SEQ ID NO.: 17 or (b) the nucleotide sequence given in SEQ ID NO.: 16.

²
~~18.~~ (Twice Amended) A nucleic acid molecule of at least 15 nucleotides in length hybridizing specifically with (a) the nucleic acid molecule of claim ¹~~17~~, (b) a nucleic acid molecule comprising SEQ ID NO.: 1, (c) a nucleic acid molecule encoding the amino acid sequence of SEQ ID NO.: 2, or (d) a sequence complementary to that of (a), (b), or (c).

cn't
D₂
³
~~19.~~ (Twice amended) A vector comprising the nucleic acid molecule of claim ~~17~~.

⁴
~~20.~~ (Amended) The vector of claim ³~~19~~, wherein the nucleic acid molecule is operatively linked to regulatory elements permitting expression in prokaryotic or eukaryotic host cells.

D₃
⁹
~~30.~~ (Amended) A method for detecting expression of a tumor suppressor in a cell by detecting the presence of mRNA coding for the tumor suppressor which comprises:
(a) obtaining mRNA from the cell;
(b) contacting the mRNA so obtained with a probe comprising a nucleic acid molecule of at least 15 nucleotides in length which, under stringent hybridizing conditions, hybridizes specifically to a nucleic acid molecule
(i) coding for the amino acid sequence of SEQ ID NO.: 2,
(ii) comprising the nucleotide sequence of SEQ ID NO.: 1,
(iii) coding for the amino acid sequence of SEQ ID NO.: 17,
(iv) comprising the nucleotide sequence of SEQ ID NO.: 16, or

- cn4
D3
- (v) having a sequence complementary to the nucleic acid molecule as defined in (i), (ii), (iii), or (iv); and
 - (c) detecting the presence of mRNA specifically hybridized to the probe, thereby detecting the expression of the tumor suppressor by the cell.
-

10/39. (Amended) A method for diagnosing in a subject a predisposition to a tumor or to a disorder associated with the expression of a tumor suppressor allele which comprises:

- D4
- (a) isolating DNA from victims of the tumor or disorder;
 - (b) digesting the isolated DNA of step (a) with at least one restriction enzyme;
 - (c) electrophoretically separating the resulting DNA fragments on a sizing gel;
 - (d) contacting the resulting gel with a probe labeled with a detectable marker comprising a nucleic acid molecule of at least 15 nucleotides in length which, under stringent hybridizing conditions, hybridizes specifically to a nucleic acid molecule
 - (i) coding for the amino acid sequence of SEQ ID NO.: 2,
 - (ii) comprising the nucleotide sequence of SEQ ID NO.: 1,
 - (iii) coding for the amino acid sequence of SEQ ID NO.: 17,
 - (iv) comprising the nucleotide sequence of SEQ ID NO.: 16, or
 - (v) having a sequence complementary to the nucleic acid molecule as defined in (i), (ii), (iii), or (iv);
 - (e) detecting labeled bands on a gel which have been hybridized to the probe as defined in (d) to create a
- 90 D

band pattern specific to the DNA of the victims of the tumor or the disorder;

- cnt
D4
- (f) preparing subject's DNA by steps (a) to (e) to produce detectable labeled bands on a gel; and
 - (g) comparing the band pattern specific to the DNA of victims of the tumor or the disorder of step (e) and the subject's DNA of step (f) to determine whether the patterns are the same or different and to diagnose thereby predisposition to the tumor or the disorder if the patterns are the same.

[Please add new claim 49 as follows:

- 3
49. (New) A method for treating, preventing, or delaying the reoccurrence of a disorder in a subject related to or dependent on the modulation of a protein comprising the amino acid sequence of SEQ ID NO.: 2 or SEQ ID NO.: 17, comprising administering to the subject an effective amount of a nucleic acid molecule of at least 15 nucleotides in length which, under stringent hybridizing conditions, hybridizes specifically to a nucleic acid molecule
- (i) coding for the amino acid sequence of SEQ ID NO.: 2,
 - (ii) comprising the nucleotide sequence of SEQ ID NO.: 1,
 - (iii) coding for the amino acid sequence of SEQ ID NO.: 17,
 - (iv) comprising the nucleotide sequence of SEQ ID NO.: 16, or
 - (v) having a sequence complementary to the nucleic acid molecule as defined in (i), (ii), (iii), or (iv).
- 91 D